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10/826,113	04/16/2004	Piotr Chomczynski	CNA / 19	1054

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/826,113	CHOMCZYNSKI, PIOTR	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 26-61* is/are pending in the application.

4a) Of the above claim(s) *1-16,26-28 and 53-58* is/are withdrawn from consideration.

5)☒ Claim(s) *62 and 63* is/are allowed.

6)☒ Claim(s) *29-39,41,42,45-52 and 59-61* is/are rejected.

7)☒ Claim(s) *40,43 and 44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

1. The objection to claim 44 is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 29-39, 41, 45-52 and 59-61 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al (Chinese patent 1,220,995, translation).

The rejection is based upon a translation of the Chen et al patent, which is attached.

Chen teaches a *method for isolating purified RNA from a biological sample* of claims 29 and 59 (see page 3, bottom half, for example or page 4) comprising:

a) *treating the sample comprising phenol at a final concentration ranging from about 10% w/w to about 60% w/w and at least one ribonuclease inhibitor* (see page 6, where 12-46% phenol is used in conjunction with guanidine isothiocyanate, an RNAse inhibitor and see page 8, preferred embodiment 2, step 1, where the phenol reagent with 30% w/w is added to the tissue),

b) mixing the sample with at least one hydrophobic solvent while maintaining a pH in the range from about pH 3.6 to below 4.0 (see page 8, preferred embodiment 2, where the pH of the phenol reagent is pH 3.5, which is about 3.6

and where the hydrophobic solvent chloroform/isoamyl alcohol is added to the solution. Further note that Chen teaches overlapping ranges of pH from 3.5 to 6.5 (see page 3)),

c) recovering the purified RNA from an aqueous phase to which about an equal volume of a water soluble organic solvent is added to precipitate the purified RNA (See page 8, preferred embodiment 2, where the aqueous phase is precipitated with isopropanol),

d) washing and solubilizing the precipitated RNA (see page 9, where the RNA precipitate is washed with alcohol and dissolved in a buffer).

With regard to claim 30, Chen teaches the use of acetate and citrate buffers (see page 8, preferred embodiment 2, lines 3 and 4).

With regard to claims 31-34, Chen teaches the use of ribonuclease inhibitors (see page 8, preferred embodiment 2, line 1, where the chaotropic salt guanidine isothiocyanate is used as an RNAse inhibitor at a concentration in the range of 0.5 M to about 6M).

With regard to claims 35-36, Chen teaches the use of detergents such as SDS and sarcosine including a range of 0.1% SDS (see page 8, preferred embodiment 2, lines 2-3).

With regard to claims 37-39, Chen teaches the use of sodium acetate and trisodium citrate, where claim 38 indicates that acetate is a preferred salt and claim 39 indicates that citrate is a preferred chelating agent).

With regard to claim 41, Chen teaches the use of Guanidine salts (see page 8, line 1).

With regard to claims 45-46, Chen teaches a pH range of 3.5-6.5 and exemplifies a pH of 3.5 (see page 3 and see page 8, preferred embodiment 2).

With regard to claims 47-49, Chen teaches the steps of:

a) treatment with the monophase reagent comprising phenol in concentrations from 12-46% w/w (see page 6) with a pH from 3.5-6.5 (see page 3) and a chaotrope (see page 6 where guandine isothiocyanate is used),

b) sedimenting the sample to obtain a purified sample substantially free of DNA, proteins and cellular components(see page 8, where the step of centrifugation is a form of sedimentation that will remove DNA, proteins and cellular components),

c) adding to the purified sample about an equal volume of a water soluble organic solvent to precipitate the purified RNA (See page 8, preferred embodiment 2, where the aqueous phase is precipitated with isopropanol),

d) sedimenting the precipitated RNA (see page 8, last sentence),

e) washing and solubilizing the precipitated RNA (see page 9, first five sentences).

With regard to claim 50, Chen teaches the use of chloroform (see page 8, middle of the page).

With regard to claim 51, Chen teaches addition of a composition which can be at "about 1.5 X" concentration (see page 8).

With regard to claim 52, 60, 61, Chen teaches precipitation with isopropanol (see page 8).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claim 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al (Chinese patent 1,220,995, translation) in view of Chomczynski (U.S. Patent 5,346,994).

Chen teaches the limitations of claim 29 as discussed above. Chen does not teach the use of a density increasing component.

Chomczynski teaches the use of glycerol in the RNA isolation buffer of Phenol/Guanidine isothiocyanate (see column 3, lines 17-32).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the isolation buffer of Chen to incorporate glycerol as taught by Chomczynski since Chomczynski notes "Furthermore, the solvent solution may include an additional solubilizer for maintaining the phenol in solution, especially at 4 C, and to achieve or maintain the solvent as a monophase solution. One suitable solubilizer is glycerol (see column 3, lines 17-24)." An ordinary practitioner would have been motivated to include glycerol in the isolation buffer of Chen in order to

maintain the phenol in solution and to assist in maintaining the solution in a monophasic form.

6. The rejection of claim 44 under 35 U.S.C. 103(a) as being unpatentable over Chen et al (Chinese patent 1,220,995, translation) in view of Puissant et al(Biotechniques (1990) 8(2):148-149) is withdrawn in view of the amendment.

Allowable Subject Matter

7. Claims 40, 43 and 44 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. Claims 62 and 63 are allowed.

9. The following is a statement of reasons for the indication of allowable subject matter: Claims 40, 43, 62 and 63 are drawn to the use of particular phenol derivatives or particular organic compounds in the RNA isolation buffer. The search did not identify any prior art which taught or suggested the use of the specific chemical compounds listed in RNA (or nucleic acid) isolation. With regard to claim 44, while Puissant teaches the pretreatment step with Guanidine, Puissant never suggests a pH of less than 4.0.

Response to Declaration

10. The Declaration under 37 CFR 1.132 filed January 17, 2007 is insufficient to overcome the rejection of claims 29-39, 41, 45-52 and 59-61 based upon 35 U.S.C. 102 as set forth in the last Office action for the following reasons.

This is not a situation where the examiner proposes to dispute the facts shown in the declaration. The examiner accepts, without reservation, that the Declarant (who is

the applicant) has shown that the particular embodiments of Chen at pH 3.5 and at pH 6.5, using the particular components of Chen, produce a significantly greater signal in the RT-PCR reaction than the embodiment of applicant, which was at pH 3.8. The issue is whether this showing is sufficient to overcome Chen as a 102 or 103 type teaching when the claims lack a limitation distinguishing the range of Chen. That is, Chen teaches embodiments which literally fall within the scope of the claim, where the only distinction is based upon the limitation "purified RNA" where the RNA is "substantially undegraded and free of DNA contamination". No specific limit is placed upon how free of DNA contamination is "substantially free".

This fact pattern is very close to two cases decided by the Federal Circuit in the last few years. Both of the cases show that in order to overcome prior art with overlapping ranges, or which in the current case anticipate the claimed ranges, the claims must be commensurate in scope with the unexpected result. In In re Harris, 74 USPQ2d 1951, 1955 (Fed. Cir. 2005), the Federal Circuit noted

> "The Board also correctly reasoned that the showing of unexpected results is not commensurate in scope with the degree of protection sought by the claimed subject matter because the elemental composition of CMSX®-486 is at or near the midpoint of the claimed range. While Harris's evidence may show a slight improvement over some alloys, the record does not show that the improved performance would result if the weight-percentages were varied within the claimed ranges. Even assuming that the results were unexpected, Harris needed to show results covering the scope of the claimed range. Alternatively Harris needed to narrow the claims."

This fact pattern is similar to the current case. The results shown in this declaration do not cover the scope of the claimed range of either the pH or of the detergent concentrations, both of which Applicant appears to believe are the critical components which differentiate the prior art. The showing a pH 3.8 is persuasive that there is an unexpected result at pH 3.8 using the claimed concentration of detergent. However, there is no evidence on the record that this result will occur at pH 3.5, pH 3.6 or pH 3.95, all of which are within the claimed range. In fact, the declaration provides some evidence that pH 3.5 of Chen is nonfunctional, which renders the claim problematic since the "about pH 3.6" language, if it means anything, means to encompass pH 3.5. Similarly, while the discussion on the detergent issue is helpful, it also fails to address the claims as filed. Only one claim addresses the amount of detergent, and that claim does not limit the total detergent amount, but simply limits the amount of one of the detergents in the mixture.

In accord with Harris is In re Peterson, 65 USPQ2d 1379, 1383 (Fed. Cir. 2003) which quotes "Establishing that one (or a small number of) species gives unexpected results is inadequate proof, for 'it is the view of this court that objective evidence of non-obviousness must be commensurate in scope with the claims which the evidence is offered to support." Here, where only one species is shown to give unexpected results, this is inadequate for a claim which broadly encompasses a much larger number of species, including the actual embodiments of the prior art of Chen itself.

Therefore, while the Declaration is believed to be factually accurate, it does not suffice to demonstrate the unexpected result because the showing itself is not

commensurate in scope with the claims, which are much broader and encompass many more ranges than those shown.

Response to Arguments

11. Applicant's arguments filed January 17, 2007 have been fully considered but they are not persuasive.

As discussed in the response above, Chen is maintained because the showing of the declaration is not commensurate in scope with the claims.

With regard to claim 59, Guanidine and Chloroform are "water soluble organic solvents" which are present in the Chen reference. There is no requirement in the claims that the separation occur without phase separation. Therefore, the argument is not commensurate in scope with the claim.

Applicant's argument with regard to the Puissant rejection was found persuasive as mentioned above and this claim is no longer rejected.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jeffrey Fredman
Primary Examiner
Art Unit 1637
2/8/07